Letters to the Editor

ULTRASOUND SCREENING IN PREGNANCY: A RANDOMISED CONTROLLED TRIAL

SIR,—The US National Institutes of Health have published a draft consensus statement on the use of ultrasound imaging in pregnancy. The panel stated that there was no evidence that the routine use of ultrasound examinations for all pregnancies improved perinatal outcome or decreased morbidity or mortality. They asked for randomised controlled trials of routine ultrasound screening in pregnancy to clarify this issue.

During 1979 and 1980 such a study was conducted in Ålesund, Norway, in one obstetrics department serving a population of about 85 000 people in a geographically well-defined area. During this period half the pregnant women in the area were randomly selected to have two routine ultrasound scans (cases). The other half were not examined routinely but could be referred for ultrasound examination on a clinical indication (controls). The cases had, besides regular obstetric care, an ultrasound examination in the 18th week (to measure fetal biparietal diameter [BPD], assess gestational age, locate the placenta, determine number of fetuses, and detect possible malformations) and in the 32nd week (for measurement of BPD and abdominal diameters for fetal growth control and for final location of the placenta and detection of malformations). 1628 women were randomised (809 cases, 819 controls). Pregnancy care was shared by the hospital obstetricians and by general practitioners as is usual in Norway. The ultrasound examinations were done by two experienced obstetricians. The doctors in the area were experienced with the possibilities of ultrasound diagnosis.

There were no differences between the groups in factors such as age, marital status, education, smoking, or parity. 14% of controls were referred for outpatient ultrasound examinations; about 12% had an ultrasound scan after hospital admission for a clinical problem.

There were 3 perinatal deaths among the cases and 8 among the controls ($p=0\cdot11$). 1 fetus of adequate size among the cases died in utero in the 40th week after a period of hyperactivity; no cause could be found. 2 other mothers (cases) admitted in the middle of the last trimester with severe pre-eclampsia lost their fetuses, which were both below the 2·5 centile weight for gestation. Among the controls, 4 of the lost fetuses represented undetected growth retardation with sudden intrauterine death (3 below the 2·5 centile and 1 below the 5 centile weight for gestation); 2 fetuses died in the 30th week, 1 of a severe malformation affecting the thorax and limbs and 1 for no specific reason; postnatally, 1 twin died of prematurity (800 g) and 1 newborn baby died with hydrops fetalis. Late neonatal deaths (death before the 28th day) numbered nil among the cases and 3 among the controls.

It is important from a socioeconomic point of view to find out if ultrasound screening will increase the use of hospital resources and thus increase the total cost of pregnancy care. No such consequences could be demonstrated: 184 cases and 269 controls were admitted to hospital ($p<0\cdot01$) for totals of 828 and 829 days respectively (10 of the cases, contributing 236 or 28% of the hospital days, were admitted because of fetal growth retardation detected by ultrasound). The routine use of ultrasound early in pregnancy to estimate the gestational age led to a significant reduction in treatment for "overdue pregnancy" (beyond the 293rd completed day), the frequency being 1·9% in cases and 7·8% in the controls ($p<0\cdot01$), and to a significant reduction in morbidity among cases after treatment for "overdue pregnancy", manifest as fewer days of inpatient care on a neonatal ward (15 days among the cases and 55 among the controls; $p<0\cdot01$). 4 of the fetuses among the controls induced for overdue pregnancy were judged premature by the paediatrician. Of the days of inpatient care in the paediatric department there were 14 in the ultrasound group and 160 among the controls in connection with malformations ($p<0\cdot01$). There were 71 days of hospital stay for hyperbilirubinaemia in the ultrasound group and 104 among the controls ($p<0\cdot05$). Severe growth retardation was recognised in the ultrasound group and this led to more active obstetric intervention of these fetuses at risk, causing more postnatal days of hospital care for dysmaturity, but this also resulted in fewer deaths due to growth retardation in the ultrasound-screened group.

All the multiple pregnancies in the ultrasound group were detected in the 18th week and the average birthweight of these fetuses was 2600 g; among the controls the average birthweight of multiple fetuses was 2180 g ($p>0\cdot05$).

Two lethal malformations were detected at the first scan among the cases and these pregnancies were terminated. 1 small myelomeningocele was overlooked. This baby was operated upon and now has a minor motor disability in the legs. Among the controls, 1 fetus (mentioned in the perinatal statistics) died and 1 born at term died in the late neonatal period after surgery for abdominal malformation.

This prospectively randomised study has demonstrated that the use of ultrasound screening in an area with experience with antenatal ultrasound diagnosis did not cause any increased use of hospital resources; it reduced the perinatal deaths and decreased morbidity. The diagnosis of severe growth retardation in the ultrasound-examined group had significant consequences. Full details of this study will be published elsewhere.

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OMEPRAZOLE: NO EVIDENCE FOR FREQUENT HEPATIC REACTIONS

SIR,—In 10 of 32 patients with duodenal ulcer treated with 20 mg or 60 mg omeprazole once daily for 4 weeks in a clinical trial[1] serum alanine aminotransferase levels (AlaT) rose from normal before the trial to values above the reference range. These increases did not seem to be due to alcohol abuse, concomitant disease, or the analytical procedures. The rises in AlaT were usually transient, slight, and asymptomatic and did not appear to be dose-related. Although these findings were not in accord with other studies[2,3] or with data on the manufacturer's files we felt that a possible toxic effect of omeprazole on liver function ought to be more fully investigated. We report here a double-blind, placebo-controlled tolerance test in sixty healthy individuals.

Forty-five men and fifteen women, thirty from Uppsala and thirty from Mölndal/Göteborg, were studied with their informed consent and with the approval of the local ethical committees. The volunteers were randomised to omeprazole 40 mg once daily for two weeks orally as hard gelatin capsules containing enteric-coated granules or to placebo capsules. Alcohol was prohibited in the week before and during the study period. The volunteers were also requested to keep their physical activity and smoking habits constant.

Blood samples were taken before the study and on days 8 and 15, after an overnight fast and before any drug administration. Enzyme assays and bilirubin measurements were done at the Sahlgrenska

1 Gustavsson S, Adami H-O, Loof L, Nyberg A, Nyrén O. Rapid healing of duodenal ulcers with omeprazole. Double blind dose-comparative trial. *Lancet* 1983, ii 124–25

TABLE I—SERUM LEVELS OF AMINOTRANSFERASES, ALKALINE PHOSPHATASE, AND TOTAL BILIRUBIN IN HEALTHY VOLUNTEERS GIVEN 40 mg OMEPRAZOLE (O) (n = 30) OR PLACEBO (P) (n = 30) DAILY FOR TWO WEEKS· MEAN±SEM

	Pretreatment		Day 8		Day 15	
Variable	O	P	O	P	O	P
AlaT	0·31±0·02	0·31±0·02	0·32±0·03	0·33±0·03	0·35±0·03	0·32±0 02
AsaT	0·34±0·02	0·33±0·02	0·32±0 02	0·33±0·02	0·33±0·02	0·32±0·02
AlP	2·4±0·1	2·5±0·1	2·4±0·1	2·4±0·1	2·4±0·1	2·4±0·1
Bilirubin	8·8±0·6	9·4±0·7	9·3±0·6	9·9±0·7	9·0±0·6	10·4±0·7

Alanine (AlaT) and aspartate (AsaT) aminotransferases and alkaline phosphatase (AlP) measured in μkat/l (1 μkatal = 60 IU) Bilirubin in μmol/l.